

Increasing use and accessibility of anti parasitic drugs for migrants with neglected diseases at a time of migratory emergency

Giovanni Cenderello¹, Antonio Di Biagio², Niccolò Riccardi², Lucia Taramasso², Andrea De Maria², Giovanni Cassola¹, Claudio Viscoli²

¹Infectious Diseases Unit, EO Ospedali Galliera, Genoa, Italy;

²Infectious Diseases Unit, IRCCS AOU San Martino-IST, University of Genoa, Genoa, Italy

SUMMARY

This work focused on *Schistosoma* spp. as a potential agent of gross haematuria in non endemic areas. This change in epidemiology is mainly due to recent migratory flows. Moreover it emphasized the need for cultural action (aimed at Urologists, Dermatologists, General Practitioners and Emergency Medicine doctors) to provide the elements for a correct and timely diagnosis. But the most important issue raised by this paper is the call for a fast track supply of drugs (usually not available in Italy) to field operators for treating tropical diseases.

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Schistosomiasis is a widespread infection in Sub-Saharan Africa, which may affect the urinary and gastro-intestinal systems. The typical signs and symptoms are abdominal pain, diarrhoea, bloody stools and haematuria. The chronic untreated infection could remain asymptomatic for years, but it can in some cases lead to severe complications such as liver damage, portal hypertension, chronic renal insufficiency and bladder cancer (Clerinx *et al.*, 2011). The European Network on Imported Infectious Disease Surveillance reports about 51,000 cases per year (Grobusch *et al.*, 2003) mainly in travellers (Gautret, 2010). This is probably an underestimation of the real number of cases, partially due to the lack of awareness and systematic screening among subjects at risk.

Praziquantel, the drug of choice for the treatment of schistosomiasis (Kramer *et al.*, 2014), is not licensed for human use in Italy and needs to be imported on a named patient basis when charged on National Health Service provision.

In Italy to date, all observed cases came from endemic areas, predominantly restricted to travellers returning from Africa and Asia (Grobusch *et al.*, 2003; Poddighe *et al.*, 2013) and asylum seekers, as recently described by Ceccarelli *et al.* (Ceccarelli *et al.*, 2013). In previous years, cases of schistosomiasis used to be seen very rarely in the metropolitan area of Genoa. For example, in 2013 and 2014 only 10 patients had been observed (5 patients/year), as shown by a retrospective review of medical records and praziquantel provision reports. From January

1st until June 31st 2015, about 291,302 people from the West Mediterranean sea campaign (Triton - Frontex) (European Parliament website, 2015) were hosted in Italy. Of them, 1,025 were relocated to Genoa, the majority originating from Mali and Senegal, the countries with the highest prevalence of schistosomiasis (Lai *et al.*, 2015). During this period, we observed a small but significant cluster of urinary schistosomiasis occurring in migrants coming to Europe through the Sicily Channel (Cenderello *et al.*, 2016). From mid-July to the 10th August, 12 patients presented to clinical observation for different signs and symptoms (lymphadenopathy, hypereosinophilia, urticaria, fever and gross haematuria) at the two main general hospitals in Genoa (Ospedale Galliera and IRCCS San Martino-IST) and referred to Infectious Disease consultants. Given the clinical and epidemiological context, a parasite search on fresh urine samples was performed and a diagnosis of schistosomiasis was obtained since all samples were positive for *Schistosoma haematobium*. Praziquantel was obtained and patients were treated with a dose of 40 mg/kg once-a-day (Kramer, 2014) with a regression of symptoms.

In a compact five-week time-frame the annual consumption of praziquantel doubled abruptly, generating major supply problems, worsened by a period of summer holidays.

The aim of the present report is to focus attention on two aspects of the dramatic ongoing migration into Europe. First, host European countries need to provide a ready circulation of drugs for the treatment of tropical diseases endemic in migrating populations, but otherwise rare in our geographic area. Aside from praziquantel, other drugs commonly used in the treatment of tropical diseases (e.g Strongyloidiasis, Filariasis) should be easily accessible. Drugs such as ivermectine, diethylcarbamazine and artesunate are not readily available in Italy and must be obtained abroad. Hospitality policies in Italy need to be

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Corresponding author:

Dr. Giovanni Cenderello

E-mail: giovanni.cenderello@galliera.it

improved to include the registration of these drugs, that should be available and distributed within the National Health Services, thus improving patient treatment and health worker efficiency.

Second, there is a need for increased awareness for schistosomiasis among general practitioners, urologists, dermatologists and emergency doctors facing migrants from endemic areas. Not only schistosomiasis, but also other non endemic diseases could show an increased incidence over the next months or years in the European Union. In addition to schistosomiasis, another likely example could be a rise in the incidence and prevalence of cutaneous and visceral leishmaniasis through the migratory flow from Syria and the Middle East (Mockenhaupt *et al.*, 2016). These diseases are otherwise relatively rare in Europe, with the exception of the area surrounding the Mediterranean basin, and may have a sharp increase in new incident and prevalent cases (Mockenhaupt *et al.*, 2016). Furthermore our clinical evidence is in line with recent data supporting the inclusion of schistosomiasis serology among the screening tests for migrants (Monge-Maillo *et al.*, 2016). In fact, the early treatment of *Schistosoma* spp. infection not only reduces the risk of cancer development, but could also reverse some cases of otherwise already established liver fibrosis (Doehring-Schwerdtfeger *et al.*, 1992). In particular, serologic assays have a significantly higher sensitivity than microscopy (Lifson *et al.*, 2002; Posey *et al.*, 2007), and could represent the future recommended approach. Along this line, the introduction of screening stool tests for ova and intestinal parasites should be considered in Sub Saharan and Syrian refugees, because of the high prevalence recently reported in these populations (Lifson *et al.*, 2002; Garg *et al.*, 2005; Mockenhaupt *et al.*, 2016). Therefore, a European concerted action or network may be needed to collect these data and share knowledge to improve the clinical care of these people. This applies in particular to our National Health Service, where a consistent margin for improvement may be detected from the present report. A correct migration policy should also include the opportunity for prompt diagnosis and appropriate and timely treatment.

References

- Ceccarelli G., d'Ettorre G., Riccardo F., Ceccarelli C., Chiaretti M., Picciarella A., *et al.* (2013). Urinary schistosomiasis in asylum seekers in Italy: an emergency currently undervalued. *J Immigr Minor Health*. **15**, 846-850.
- Cenderello G., Taramasso L., Riccardi N., Di Biagio A., Cassola G., De Maria A. (2016). Chemotherapy Mass Campaigns and Migratory Flows: An Unexpected Connection. *Clin Infect Dis E-pub ahead of print pii:ciw087*
- Clerinx J., Van Gompel A. (2011). Schistosomiasis in travellers and migrants. *Travel Med Infect Dis*. **9**, 6-24.
- Doehring-Schwerdtfeger E., Abdel-rahim I.M., Kardoff R., Kaiser C., Franke D., Schlake J., *et al.* (1992). Ultrasonographical investigation of periportal fibrosis in children with *Schistosoma mansoni* infection: reversibility of morbidity twenty-three months after treatment with praziquantel. *Am J Trop Med Hyg*. **46**, 409-415.
- <http://www.europarl.europa.eu/EPRS/EPRS-AaG-565905-Recent-Migration-flows-to-the-EU-FINAL.pdf>
- Garg P.K., Perry S., Dorn M., Hardcastle L., Parsonnet J. (2005). Risk of intestinal helminth and protozoan infection in a refugee population. *Am J Trop Med Hyg*. **73**, 386-391.
- Gautret P., Cramer J.P., Field V., Caumes E., Jensenius M., Gkrania-Klotsas E., *et al.* (2012). Infectious diseases among travellers and migrants in Europe, EuroTravNet 2010. *EuroSurveill*. **17**, pii=20205.
- Grobusch M.P., Mühlberger N., Jelinek T., Bisoffi Z., Corachán M., Harms G., *et al.* (2003). Imported schistosomiasis in Europe: sentinel surveillance data from Trop Net Europ. *J Travel Med*. **10**, 164-169.
- Kramer C.V., Zhang F., Sinclair D., Olliaro P.L. (2014). Drugs for treating urinary schistosomiasis. *Cochrane Database Syst Rev*. **8**, CD000053.
- Lai Y.S., Biedermann P., Ekpo U.F., Garba A., Mathieu E., Midzi N., *et al.* (2015). Spatial distribution of schistosomiasis and treatment needs in sub-Saharan Africa: a systematic review and geostatistical analysis. *Lancet Infect Dis*. **15**, 927-940.
- Lifson A.R., Thai D., O'Fallon A., Mills W.A., Hang. (2002). Prevalence of tuberculosis, hepatitis B virus, and intestinal parasitic infections among refugees to Minnesota. *Public Health Rep*. **117**, 69-77.
- Mockenhaupt F.P., Barbre K.A., Jensenius M., Larsen C.S., Barnett E.D., Stauffer W., *et al.* (2016). Profile of illness in Syrian refugees: a Geo-Sentinel analysis, 2013 to 2015. *Euro Surveill*. **21**.
- Monge-Maillo B., López-Vélez R., Norman F.F., Ferrere-González F., Martínez-Pérez Á., Pérez-Molina J.A. (2015). Screening of imported infectious diseases among asymptomatic sub-Saharan African and Latin American immigrants: a public health challenge. *Am J Trop Med Hyg*. **92**, 848-856.
- Poddighe D., Castelli L., Pulcrano G., Grosini A., Balzaretto M., Spadaro S., Bruni P. (2015). Urinary Schistosomiasis in an Adolescent Refugee from Africa: An Uncommon Cause of Hematuria and an Emerging Infectious Disease in Europe. *J Immigr Minor Health*. [E pub ahead of print]. Pubmed PMID 26335551.
- Posey D.L., Blackburn B.G., Weinberg M., Flagg E.W., Ortega L., Wilson M., *et al.* (2007). High prevalence and presumptive treatment of schistosomiasis and strongyloidiasis among African refugees. *Clin Infect Dis*. **45**, 1310-1315.